Day : Thursday
Date: 9/27/2007

Time: 16:55:49

PALM INTRANET

Inventor Information for 10/500999

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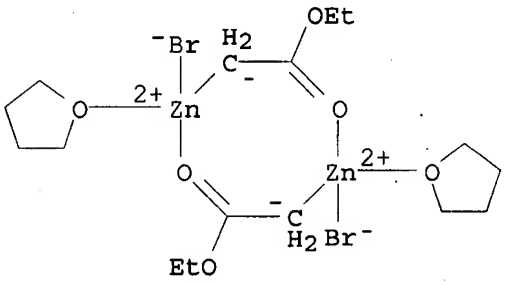
9/27/07

SRNT

L2 ANSWER 2 OF 127 REGISTRY COPYRIGHT 2007 ACS on STN
RN 566935-35-1 REGISTRY
ED Entered STN: 15 Aug 2003
CN Zinc, dibromobis[μ-[2-ethoxy-2-(oxo-κO)ethyl-κC]]bis(tetrahydrofuran)di-, stereoisomer (9CI) (CA INDEX NAME)
MF C16 H30 Br2 O6 Zn2
CI CCS
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L2                STR
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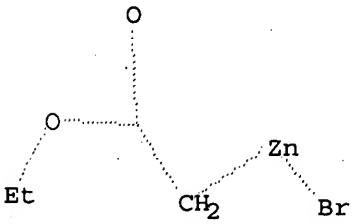

Structure attributes must be viewed using STN Express query preparation.

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L1                SCREEN 963
L2                STRUCTURE UPLOADED
L3                QUE L2 AND L1
L4             0 S L2
L5             5 S L2 FUL
L6          1969 S ZN/ELS (P) BR/ELS (P) O/ELS (P) C/ELS
L7             5 S L5 AND CAPLUS/LC
L8             1 S L5 AND REF.CAPLUS>10
L9             4 S L5 NOT L8

     FILE 'ZCAPLUS' ENTERED AT 14:33:43 ON 27 SEP 2007
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L11           78 S L8
L12            4 S L8 AND (?CRYSTAL?)
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9/27/07

The Structure of the Reformatsky Reagent

Jan Dekker, Jaap Boersma,* and Gerrit J. M. van der Kerk
Laboratory for Organic Chemistry, State University, Croesestraat 79, 3522 AD Utrecht, The Netherlands

The Reformatsky reagent '$BrZnCH_2CO_2R$' is a cyclic dimer with bridging $-CH_2C(OR)O-$ groups.

The Reformatsky reaction (1) has been used in synthetic organic chemistry for almost a century. Although various preparative aspects of this reaction have been explored extensively,[1] only little is known about the true nature of the intermediate (**1**), the Reformatsky reagent. Both *C*-metallated (**1a**) and *O*-metallated (**1b**) species have been proposed on the

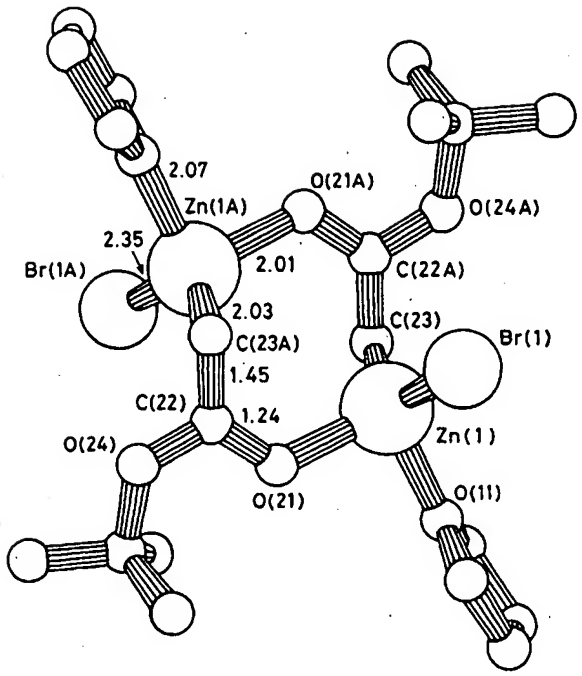

Figure 1. Crystal structure of $(BrZnCH_2CO_2Bu^t \cdot THF)_2$, with bond lengths in Å, showing the crystallographic numbering system; bond angles are O(21)–C(22)–C(23A), 124.8; C(22)–C(23A)–Zn, 108.9; C(23A)–Zn–O(21A), 111.0; Zn–O(21A)–C(22A), 125.5°.

basis of spectroscopic data.[2–4] However, no molecular structures, either in solution or in the solid state, have been established.

$$BrCH_2CO_2R + Zn \rightarrow (1) \xrightarrow[\text{ii, } H_3O]{\text{i, } R'_2CO} R'_2C(OH)CH_2CO_2R \quad (1)$$

$BrZnCH_2CO_2R$ (1a) $\qquad$ $CH_2{=}C(OR)OZnBr$ (1b)

In our exploration of organozinc co-ordination chemistry, we have been studying the classical Reformatsky reagent (1) derived from $BrCH_2CO_2Et$. Since no single crystals of this species could be obtained, this study had to be confined to the characterization of the species in solution. Recently Orsini *et al.*[4] reported that the Reformatsky reagent prepared from zinc and $BrCH_2CO_2Bu^t$ in tetrahydrofuran (THF) was a microcrystalline compound. We have grown single crystals of this compound and determined its structure by *X*-ray diffraction analysis.

Crystal data: monoclinic, space group $P2_1/n$, $a = 10.322$, $b = 12.357$, $c = 11.654$ Å, $\beta = 112.65°$, $Z = 2$ (dimeric units). The refinement, based on a partial data set (1133 reflections), converged at an R value of 0.073.

The zinc is almost tetrahedrally surrounded by two oxygen, one bromine, and one carbon atom. The dimeric unit forms an 8-membered non-planar ring, $(ZnCCO)_2$, with normal zinc–carbon and zinc–oxygen single bond distances. This unit is depicted in Figure 1, with bond lengths and angles indicated.

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

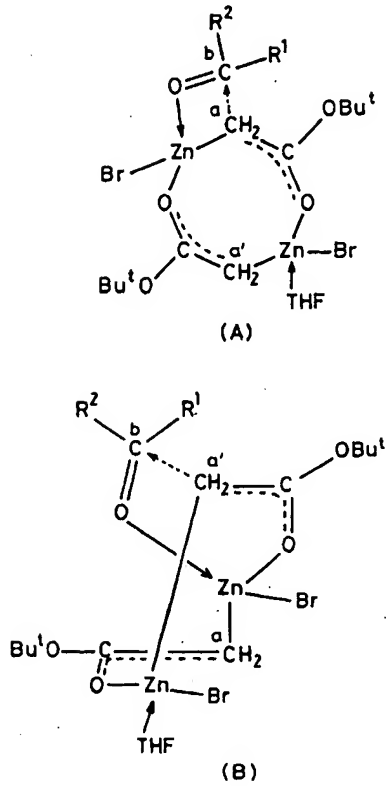

Figure 2. Proposed intermediates in the reaction of the Reformatsky reagent with a ketone. (A) Four-centre mechanism (attack of C^a on C^b). (b) Six-centre mechanism (attack of $C^{a'}$ on C^b).

A comparable 8-membered ring, $(ZnNCO)_2$, was found some years ago in the structure of methyl *N*-phenyl-*N*-ethylzinciocarbamate.[5]

Ebulliometry in THF showed that the t-butyl compound retains its dimeric structure in this solvent. The corresponding reagent derived from $BrCH_2CO_2Et$ is also a dimer in THF, dioxan, and pyridine. Moreover, the n.m.r. spectra of both reagents in THF, Me_2SO, and pyridine show in each case almost identical chemical shifts for the CH_2 group bound to zinc. We therefore believe that this dimeric structure is the basic structure of the Reformatsky reagent. For this reason it is, in our opinion, incorrect to describe the reagent as either a *C*-metallated[4] or an *O*-metallated[2] mononuclear species.

Any mechanism operative in the Reformatsky reaction (1) must take into account the dimeric structure of the reagent. The first step will undoubtedly be the displacement of a co-ordinated solvent molecule by a carbonyl compound. In the second step the carbonyl group can react either with the CH_2 group of the zinc atom to which it is co-ordinated in a four-centre mechanism (Figure 2A), or with the CH_2 group attached to the other zinc atom of the dimer in a six-centre mechanism (Figure 2B). The first possibility is analogous to the mechanism proposed by Ashby and Bowers[6] for the formation of the 1,2-addition product in the reaction of Grignard reagents with benzophenone. The second one resembles the mechanism for the Reformatsky reaction proposed by Mousseron *et al.*[7]

A model study shows that more steric hindrance occurs between the carbonyl compound and the dimeric reagent in the four-centre mechanism than in the six-centre mechanism. Moreover, in the six-centre mechanism the carbonyl group can more easily approach the carbon atom to which it is going to be attached. On the basis of these considerations, we prefer the six-centre mechanism.

We are grateful to Dr. A. L. Spek and Mr. A. J. M. Duisenberg for the collection of the *X*-ray data.

Received, 20th January 1983; Com. 094

References

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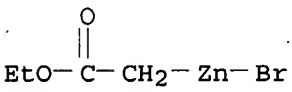
L12 ANSWER 3 OF 4 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:575948 ZCAPLUS
DOCUMENT NUMBER: 99:175948
TITLE: The structure of the Reformatskii reagent
AUTHOR(S): Dekker, Jan; Boersma, Jaap; Van der Kerk, Gerrit J. M.
CORPORATE SOURCE: Lab. Org. Chem., State Univ. Utrecht, Utrecht, 3522 AD, Neth.
SOURCE: Journal of the Chemical Society, Chemical Communications (1983), (10), 553-5
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English

AB X-ray diffraction anal. showed that the Reformatskii reagent prepared from Zn and BrCH2CO2CMe3 in THF is (BrZnCH2CO2CMe3.THF)2. NMR studies suggest that the corresponding reagent prepared from BrCH2CO2Et is (BrZnCH2CO2Et)2. This dimeric structure is proposed as the basic structure of the Reformatskii reagent.

IT **5764-82-9**
RL: PRP (Properties)
(structure of)

RN 5764-82-9 ZCAPLUS
CN Zinc, bromo(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



CC 29-9 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 23, 75

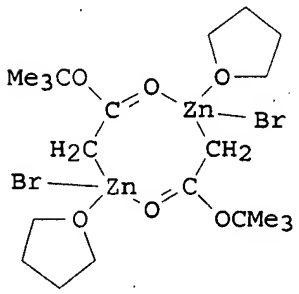
ST Reformatskii reagent **crystal** structure; zinc bromoacetate reaction product structure

IT **Crystal** structure
Molecular structure
(of Reformatskii reagent)

IT 87654-00-0
RL: PRP (Properties)
(**crystal** structure of)

IT **5764-82-9**
RL: PRP (Properties)
(structure of)

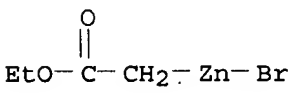
L12 ANSWER 2 OF 4 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:511077 ZCAPLUS
DOCUMENT NUMBER: 101:111077
TITLE: The nature of the Reformatsky reagent. Crystal structure of (BrZnCH2COO-t-Bu.THF)2
AUTHOR(S): Dekker, Jan; Budzelaar, Peter H. M.; Boersma, Jaap; Van der Kerk, Gerrit J. M.; Spek, Anthony J.
CORPORATE SOURCE: Org. Chem. Lab., Univ. Utrecht, Utrecht, 3522, Neth.
SOURCE: Organometallics (1984), 3(9), 1403-7
CODEN: ORGND7; ISSN: 0276-7333
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The Reformatskii reagents derived from BrCH2CO2R (R = Et, Me3C) were studied by association measurements and NMR spectroscopy in various solvents. The reagents were dimeric in all but the most polar solvents. The x-ray crystal structure of (BrZnCH2CO2CMe3·THF)2 (I) showed it has a dimeric structure containing both Zn-O and Zn-C single bonds. The dimeric structure found in the crystal persisted in solution In the very polar solvent Me2SO, the reagents were monomeric C-metalated species. The consequences of these findings for the mechanism of the Reformatskii reaction in the commonly used solvents were discussed.

IT 5764-82-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(NMR and structure of)
RN 5764-82-9 ZCAPLUS
CN Zinc, bromo(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



CC 29-9 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 75
ST crystal structure Reformatskii reagent; mol structure Reformatskii reagent; NMR Reformatskii reagent
IT Crystal structure
(of Reformatskii reagent)

IT 5764-82-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(NMR and structure of)
IT 90528-93-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)